Amendments to Specification

Please replace the paragraph beginning on page 8, line 18 with the following paragraph:

Mitochondrial mutations are determined with reference to wild-type human mitochondrial sequence. Sequence information can be found at the website ~~http://www.gen.emory.edu/mitomap.html~~ gen.emory.edu/mitomap.html and at SEQ ID NO: 1. However, some differences between a sample sequence and a documented wild-type sequence can be polymorphisms, not mutations. Table 3 provides a number of new polymorphisms. Other polymorphisms can be found in references 2 and 8. Polymorphisms can be distinguished from somatic mutations by comparing the sequence in the sample to the corresponding sequence in a normal body tissue of the same person. If the same variant sequence is found in the sample as in the normal body tissue it is a polymorphism. Normal tissues can be paraffin-embedded. It has been found by the present inventors that mitochondrial DNA which is paraffin-embedded remains more highly intact and amplifiable than genomic DNA. Amplifiable regions of mitochondrial DNA may be from 10 bp to about 4 kb, desirably 2 kb to 4 kb or 10 bp to about 2 kb. Other suitable sources of reference mtDNA are blood, serum, or plasma of the human being tested.

Please replace the paragraph beginning on page 12, line 4 with the following paragraph:

Mutations can first be identified by comparison to sequences present in public databases for human mitochondrial DNA, e.g., at ~~http://www.gen.emory.edu/mitomap.html~~ gen.emory.edu/mitomap.html and at SEQ ID NO: 1. Any single basepair substitution identified in the sample DNA compared to a normal sequence from a database can be confirmed as being a somatic mutation as opposed to a polymorphic variant by comparing the sample mitochondrial DNA or sequences obtained from it to control cell mitochondrial DNA from the same individual or sequences obtained from it. Control cells are isolated from other apparently normal tissues, i.e., tissues which are phenotypically normal and devoid of any visible, histological, or immunological characteristics of cancer tissue. A difference between the sample and the control identifies a somatic mutation which is associated with the tumor.

Please replace the paragraph beginning on page 12, line 16 with the following paragraph:

An alternative to serially sequencing the entire mitochondrial genome in order to identify a single basepair substitution is to use hybridization of the mitochondrial DNA to an array of oligonucleotides. Hybridization techniques are available in the art which can rapidly identify mutations by comparing the hybridization of the sample to matched and mismatched sequences which are based on the human mitochondrial genome. Such an array can be as simple as two oligonucleotide probes, one of whose sequence matches the wild-type or mutant region containing the single base substitution (matched probe) and another whose sequence includes a single mismatched base (mismatch control probe). If the sample DNA hybridizes to the matched probe but not the mismatched probe, it is identified as having the same sequence as the matched probe. Larger arrays containing thousands of such matched/mismatched pairs of probes on a glass slide or microchip ("microarrays" or "gene chips") are available which are capable of sequencing the entire mitochondrial genome very quickly. Such arrays are commercially available. Review articles describing the use of microarrays in genome and DNA sequence analysis and links to their commercial suppliers are available at ~~www.gene-chips.com~~ gene-chips.com.

Please replace the paragraph on page 19, lines 4-6 with the following paragraph:

MITOMAP: A Human Mitochondrial Genome Database. Center for Molecular Medicine, Emory University, Atlanta, GA, USA.
~~http://www.gen.emory.edu/mitomap.html~~ gen.emory.edu/mitomap.html

Please replace the paragraph beginning on page 3, line 6 with the following paragraph:

According to another embodiment of the invention an oligonucleotide probe is provided. The probe comprises a sequence of at least 10 contiguous nucleotides of a human mitochondrial genome. The probe can optionally contain at least 12, 14, 16, 18, 20, 22, 24, 26, or 30 such contiguous nucleotides. The oligonucleotide comprises a mutation selected from the group consisting of: a mutation selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide ~~302~~ 303; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532;

C→T at nucleotide 150; T→C at nucleotide 195; ~~ΔC at nucleotide 302~~; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide 16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; A→G at nucleotide 16300; A→G at nucleotide 10792; C→T at nucleotide 10793; C→T at nucleotide 10822; A→G at nucleotide 10978; A→G at nucleotide 11065; G→A at nucleotide 11518; C→T at nucleotide 12049; T→C at nucleotide 10966; G→A at nucleotide 11150; G→A at nucleotide 2056; T→C at nucleotide 2445; T→C at nucleotide 2664; T→C at nucleotide 10071; T→C at nucleotide 10321; T→C at nucleotide 12519; Δ 7 amino acids at nucleotide 15642; G→A at nucleotide 5521; G→A at nucleotide 12345; T→C substitution at position 710; T→C substitution at position 1738; T→C substitution at position 3308; G→A substitution at position 8009; G→A substitution at position 14985; T→C substitution at position 15572; G→A substitution at position 9949; T→C substitution at position 10563; G→A substitution at position 6264; A insertion at position 12418; T→C substitution at position 1967; T→A substitution at position 2299; and G→A at nucleotide 3054.

Please replace the paragraph beginning on page 4, line 1 with the following paragraph:

According to another aspect of the invention an oligonucleotide primer is provided. It comprises a sequence of at least 10 contiguous nucleotides of a human mitochondrial genome. The primer can optionally contain at least 12, 14, 16, 18, 20, 22, 24, 26, or 30 such contiguous nucleotides. The oligonucleotide comprises a mutation selected from the group consisting of: a mutation selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide ~~302~~ 303; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532; C→T at nucleotide 150; T→C at nucleotide 195; ~~ΔC at nucleotide 302~~; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide 16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; A→G at nucleotide 16300; A→G at nucleotide 10792; C→T at nucleotide 10793; C→T at nucleotide 10822; A→G at nucleotide 10978; A→G at nucleotide 11065; G→A at nucleotide 11518; C→T at

nucleotide 12049; T→C at nucleotide 10966; G→A at nucleotide 11150; G→A at nucleotide 2056; T→C at nucleotide 2445; T→C at nucleotide 2664; T→C at nucleotide 10071; T→C at nucleotide 10321; T→C at nucleotide 12519; Δ7 amino acids at nucleotide 15642; G→A at nucleotide 5521; G→A at nucleotide 12345; T→C substitution at position 710; T→C substitution at position 1738; T→C substitution at position 3308; G→A substitution at position 8009; G→A substitution at position 14985; T→C substitution at position 15572; G→A substitution at position 9949; T→C substitution at position 10563; G→A substitution at position 6264; A insertion at position 12418; T→C substitution at position 1967; T→A substitution at position 2299; and G→A at nucleotide 3054.

Please replace the paragraph beginning on page 5, line 26 with the following paragraph:

Another embodiment of the invention provides a method to aid in detecting the presence of tumor cells in a patient. The presence of a mutation in a mitochondrial genome of a cell sample of a patient is determined. The mutation is selected from the group consisting of: T→C at nucleotide 114; ΔC at nucleotide ~~302~~ 303; C→A at nucleotide 386; insert T at nucleotide 16189; A→C at nucleotide 16265; A→T at nucleotide 16532; C→T at nucleotide 150; T→C at nucleotide 195; ~~ΔC at nucleotide 302~~; C→A at nucleotide 16183; C→T at nucleotide 16187; T→C at nucleotide 16519; G→A at nucleotide 16380; G→A at nucleotide 75; insert C at nucleotide 302; insert CG at nucleotide 514; T→C at nucleotide 16172; C→T at nucleotide 16292; A→G at nucleotide 16300; A→G at nucleotide 10792; C→T at nucleotide 10793; C→T at nucleotide 10822; A→G at nucleotide 10978; A→G at nucleotide 11065; G→A at nucleotide 11518; C→T at nucleotide 12049; T→C at nucleotide 10966; G→A at nucleotide 11150; G→A at nucleotide 2056; T→C at nucleotide 2445; T→C at nucleotide 2664; T→C at nucleotide 10071; T→C at nucleotide 10321; T→C at nucleotide 12519; Δ7 amino acids at nucleotide 15642; G→A at nucleotide 5521; G→A at nucleotide 12345; T→C substitution at position 710; T→C substitution at position 1738; T→C substitution at position 3308; G→A substitution at position 8009; G→A substitution at position 14985; T→C substitution at position 15572; G→A substitution at position 9949; T→C substitution at position 10563; G→A substitution at position 6264;

A insertion at position 12418; T→C substitution at position 1967; T→A substitution at position 2299; and G→A at nucleotide 3054. The patient is identified as having a tumor if one or more mutations are determined in the mitochondrial genome of the cell sample of the patient.

Please replace Table 2 on page 23 with the following table:

Table 2. Summary of mitochondrial mutations in primary tumors.

Patient#	Location	Sequence	Protein	Gene
Bladder Cancer		(9/14,57%)		
1124	114	T->C	N/C	D-loop
580	~~302~~ 303	DelC	N/C	D-loop
580	386	C->A	N/C	D-loop
799	2056	G->A	N/C	16SrRNA
716	2445	T->C	N/C	16SrRNA
1127	3054	G->A	N/C	16SrRNA
884	10071	T->C	L-L	ND3
884	10321	T->C	V-A	ND3
884	10792	A->G	L-L	ND4
884	10793	C->T	L-L	ND4
899	10822	C->T	H-H	ND4
716	10978	A->G	L-L	ND4
870	11065	A->G	L-L	ND4
870	11518	G->A	L-L	ND4
884	12049	C->T	F-F	ND4
874	12519	T->C	V-V	ND5
580	15642	Del	7aa	Cyt b
899	16189	InsT	N/A	D-loop
1124	16265	A->C	N/A	D-loop
1127	16532	A->T	N/A	D-loop
Lung Cancer		(6/15,40%)		
1174	150	C->T	N/C	D-loop
1174	195	T->C	N/C	D-loop
902	~~302~~ 303	DelC	N/C	D-loop
898	2664	T->C	N/C	16sRNA
915	5521	G->A	N/C	tRNATrp
915	12345	G->A	N/C	tRNALeu
915	16183	C->A	N/C	D-loop
915	16187	C->T	N/C	D-loop
1113	16519	T->C	N/C	D-loop
1140	16380	G->A	N/C	D-loop
Head and Neck Cancer		(6/13,46%)		
1637	75	G->A	N/C	D-loop
1680	302	Ins C	N/C	D-loop
1565	514	InsCG	N/C	D-loop
1708	10966	T->C	T->T	ND4
1678	11150	G->A	A->T	ND4
1680	16172	T->C	N/C	D-loop
1680	16292	C->T	N/C	D-loop
1680	16300	A->G	N/C	D-loop

Only D-loop region was analyzed for lung patients #1113,#1140, and #1174.